

# Acute optic neuritis

## A local management and treatment pathway

**T**here has long been a controversy about the optimal treatment of acute optic neuritis (AON). The Optic Neuritis Treatment Trial (ONTT) was set up in the late 1980s to try to clarify the role of systemic steroids, and the findings of the 10-year follow-up of this study were recently published<sup>1</sup>.

Ophthalmologists at the Royal Albert Edward Infirmary in Wigan have attempted to produce an evidence-based management protocol for AON applicable to their eye department. In order to be practicable and workable, this protocol took into account local circumstances; the ophthalmologists are based in the local district general hospital whilst the neurologists are based at a specialist centre elsewhere in the region.

### AON signs and symptoms

AON involves a sudden onset localised inflammation within the optic nerve. This is usually sited posterior to the eye and optic disc and is then referred to as retrobulbar neuritis. The cause is not known for certain. There is often a marked unilateral loss of vision within days of onset, with a subsequent recovery of vision over a period of several weeks. Many patients regain good vision but this cannot be guaranteed. There is always some permanent damage to the optic nerve with a loss of myelin around the nerve axons at the site of inflammation. It is therefore said to be a demyelinating condition.

Other symptoms may include a pain in or around the eye. This may be exacerbated by eye movement or pressure applied through the upper lid. As well as reduced visual acuity, there is impairment of colour perception, especially red, and a relative afferent pupil defect (assuming the other eye and vision are normal). Uhthoff's phenomena is where vision becomes even worse with an increase in body temperature as may occur with exercise or hot bathing. The optic disc is likely to look normal if there has been no previous attack and when the acute lesion is sited well behind the eye.

### Management controversy and variation

Historically, the main dilemma in the treatment of AON has been the role of systemic steroids. Back in the 1980s, some clinicians gave oral steroids whilst others felt that such treatment made no difference to the outcome of the condition and so did not. There was, however, an impression that such treatment might speed up visual recovery even if the ultimate degree of improvement was not altered.

In an attempt to resolve these uncertainties, the Optic Neuritis Treatment Trial (ONTT) was conducted between 1988 and 1991. As the patient groups have been followed up over the subsequent years, the findings and conclusions of this trial have shifted somewhat. Perhaps partly because of this, there is still a wide variation in the management of AON in the UK.

This variation is seen not only in the use of steroids and their mode of administration, but also in the use of magnetic resonance imaging (MRI scan) of the brain. This was highlighted by a survey of the management of AON in the north west of England<sup>2</sup>. It was found that only 9% of ophthalmologists prescribed intravenous steroids for AON compared to 55% of neurologists. Sixty-four percent of ophthalmologists did not give steroids at all, whereas only 32% of neurologists chose to do so. A brain MRI scan was ordered by 46% of neurologists but only by 36% of ophthalmologists.

### Association with multiple sclerosis

It has been known for a long time that there is an association between AON and multiple sclerosis (MS). The problem lies in predicting the future MS risk for the individual patient suffering their first attack of AON, and in deciding what to do about it. Previous studies have indicated that the overall risk of developing clinical MS following AON is around 20% within two years and between 45% and 80% within 15 years<sup>3</sup>.

For the 388 participants still under follow-up at 10 years in the ONTT, there was a 30% risk of MS at five years and a 38% risk at 10 years<sup>1</sup>. It was also found that a brain MRI scan done at the time of the original AON was helpful in predicting the risk of developing MS. If there was even a single white matter lesion on MRI scan then the 10-year risk of MS rose to 56%. Multiple MRI lesions did not appreciably increase the risk. If the MRI scan was normal, the risk was only 22%. There was also a lower risk for MS if the AON was atypical, e.g. if there was severe disc swelling, haemorrhages or exudates adjacent to the disc, an absence of pain and if the vision was reduced to mere perception of light.

### Trials

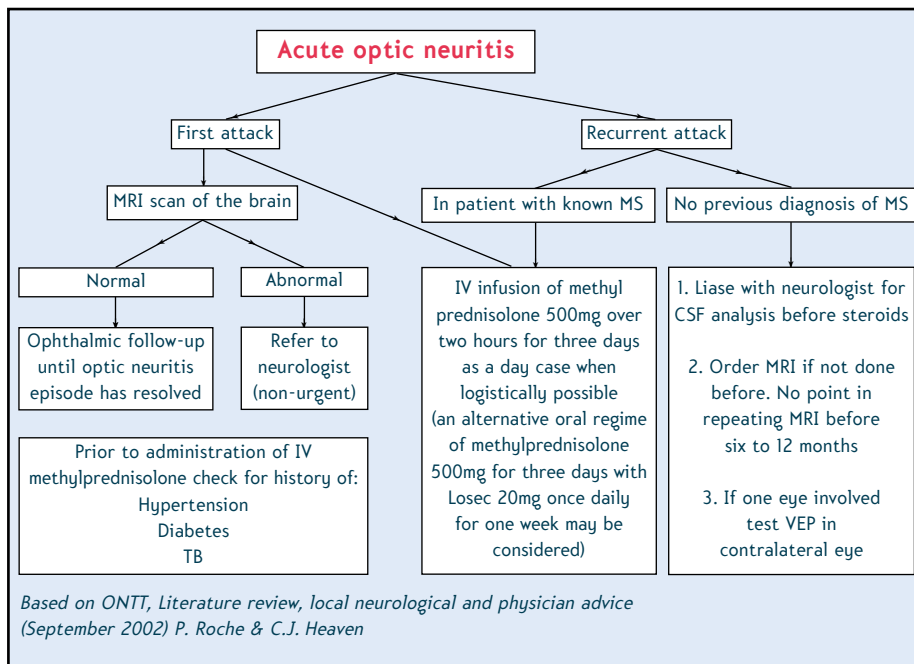
In the ONTT, conducted across 15 centres in the USA, 457 patients with AON were originally randomly allocated to one of the three treatment groups. In group one, oral prednisolone (1mg/kg/day) was given for 14 days. In group two, intravenous (IV) methylprednisolone (1mg/day, i.e. a mega dose) was given for three days followed by oral prednisolone (1mg/kg/day) for 11 days. In group three, an oral placebo was given for 14 days.

The IV methylprednisolone regime accelerated visual recovery but provided no long-term benefit to vision. Oral prednisolone alone was ineffective and increased the risk of new episodes of optic neuritis. After two years of follow-up, the IV methylprednisolone regime was found to have reduced the risk for development of MS, particularly in patients who at the start of the study had brain MRI changes consistent with demyelination<sup>3</sup>. However, by three years of follow-up, this treatment effect had subsided. This raises the question as to whether periodic courses of IV methylprednisolone might provide ongoing reduced risk of MS development/progression in susceptible patients.

As indicated earlier, patients with an abnormal brain MRI scan at the time of a first attack of AON are at higher risk of developing MS. For these patients, it has been shown that giving beta-1a interferon following the IV methylprednisolone regime further reduces the chance of developing clinically definite MS and lessens the chance of new or enlargement of MRI brain abnormalities<sup>4,6</sup>. Despite this, guidelines published by the National Institute for Clinical Excellence (NICE) in 2002 have recommended that on the basis of clinical and cost-effectiveness, beta-1a interferon is not recommended for the treatment of MS in England and Wales.

Collectively, these findings have shifted the emphasis in the management of AON from vision to brain. The message is that often AON is not an isolated phenomena but may represent one manifestation of an ongoing multi-hit disease of the CNS. This is what MS is in essence. The occurrence of an optic neuritis should therefore alert one to the need for the implementation of a treatment regime to suppress demyelination insults to the brain.

The old theory that corticosteroids may speed up visual recovery, but do not much affect visual outcome, has been found to be true. Their role in restoration of vision is limited. However (in the context of AON) IV methylprednisolone and beta-1a interferon appear to have a significant role for some in the protection of the brain



►► **Figure 1**  
Management of acute optic neuritis

from future demyelinating insults and, therefore, in preserving the general neurological integrity of the patient. If this could be extrapolated to the management of MS as a whole, it would seem logical to instigate such treatments early in the course of the condition before severe CNS damage has occurred.

### Local treatment protocol

In view of the above, and in collaboration with local neurologists, a treatment protocol for AON was devised by the Wigan ophthalmologists (Figure 1). This protocol contains some pragmatic compromises, which reflect local circumstances.

Local patients may face a significant delay before obtaining a MRI brain scan. It was therefore thought best to instigate IV methylprednisolone treatment without undue delay and ahead of the results of the MRI scan. For those who are subsequently found to have a normal brain MRI, there is less need to provide therapeutic protection of the brain but the steroid may at least speed up visual recovery for those patients. As the key issue is long-term protection of the CNS, it was not considered necessary to give the steroid treatment as an emergency. Arrangements are made to administer it as soon as is practicable and this usually means within a few days (e.g. after the weekend rather than immediately on a Friday evening). Patients attend the eye ward for two hours on three consecutive days for the treatment.

The view of the local neurologist was

that the oral prednisolone, used in the ONTT following the IV methylprednisolone, was not necessary. An alternative oral regime of methylprednisolone was also suggested should there be circumstances where the IV regime is problematic. Whether the 500mg of methylprednisolone is given IV or by mouth it is still a vastly higher dose than the oral prednisolone of 1mg per kg body weight.

Those patients with an abnormal MRI are referred on for a neurological opinion. It is left to the neurologist (at their request) to discuss the fuller implications of these findings with the patient.

A definition of MS is multiple episodes of CNS inflammatory demyelination separated in space or time. By this criterion, two episodes of AON would qualify as MS. If there has been a recurrence of AON in the absence of other clinical neurological disease, the neurologist may wish to critically assess the patient for evidence of other CNS disturbance. This may involve a lumbar puncture to analyse cerebrospinal fluid (CSF). In this scenario, the steroid regime is withheld as it might affect the result of this investigation. Also if the vision of only one eye has been affected, a visually evoked response (VER) may be performed to test for slow conduction in the fellow optic nerve. If found, this would add weight to the possibility of the patient having MS.

In view of the NICE guidelines, ophthalmologists are not able to prescribe beta-1a interferon.

### Conclusion

This protocol works well in practice. Its implementation has improved the management of the patient in a number of ways. There is now an evidence-based standardisation of care within the eye department. There has been a clarification in the division of responsibility in the shared care of the patient between the ophthalmologist and neurologist, and a generally improved level of liaison between the ophthalmologists and the local neurological service.

It should be emphasised that this precise protocol may not suit all local neuro-ophthalmological services. However, it may help reduce the variation in the management of AON in the UK.

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